REMARKS

I. Status of the Claims

Claims 1-38 were originally filed in the parent application. In the preliminary amendment submitted with this application, claims 1-11 and 19-38 were canceled. Claims 12-18 remain pending under examination. Upon entry of the present amendment, claim 15 is canceled. Claim 12 is amended to replace the term "Kv10" with the term "Kv," which is present in this claim as originally filed. Claims 12 and 13 are amended to recite that the claimed polypeptide comprises an amino acid sequence having at least 90% or 95% sequence identity to SEQ ID NO:3, which finds support in the specification, *e.g.*, on page 12, lines 26-33. Claim 18 is amended to ensure proper antecedent basis. No new matter is introduced.

II. Information Disclosure Statement

The Examiner objected to the information disclosure statement submitted on March 31, 2004, and indicated that references AE-AG and AL had not been considered. Applicant hereby re-submits the relevant references.

III. Claim Rejections

A. 35 U.S.C. §101

Claims 12-18 were rejected under 35 U.S.C. §101 for alleged lack of patentable utility. The Examiner stated that the claimed invention has no apparent or asserted specific and substantial credible utility. Applicant respectfully traverses the rejection.

The Standard for Assessing Utility

According to MPEP §2107, the Examiner should review the claims and the supporting written description to determine whether the utility requirement under 35 U.S.C. §101 is met. No rejection based on lack of utility should be made if an invention has a well-established utility, *i.e.*, a utility that will be immediately appreciated by one of ordinary skill in the art based on the characteristics of the invention, regardless of whether any such utility has been asserted. Neither should any rejection be made for lack of utility if an applicant has

asserted a specific and substantial utility that would be considered credible by one of ordinary skill in the art.

In most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101. MPEP §2107.02 III A. The Court of Customs and Patent Appeals stated in *In re Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of §101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

In re Langer, 183 USPQ 288, 297 (CCPA, 1974, emphasis in original). To overcome the presumption of sufficient utility as asserted by an applicant, the Examiner must carry the initial burden to make a *prima facie* showing of lack of utility and provide a sufficient evidentiary basis for the conclusion. In other words, the Examiner "must do more than merely question operability--[he] must set forth factual reasons which would lead one skilled in the art to question objective truth of the statement of operability." *In re Gaubert*, 187 USPQ 664, 666 (CCPA 1975).

MPEP §2107.02 IV further states, a detailed explanation should be given for a utility rejection as to why the claimed invention has no specific and substantial asserted utility. Documentary evidence should be provided when possible. Otherwise the Examiner should specifically explain the scientific basis for his factual conclusions.

The Asserted Utility Is Specific, Substantial, and Credible

The instant application asserts a specific and substantial utility of the claimed invention. For example, it is asserted on page 3, lines 2-11, and on page 8, line 14, to page 9, line 7, that Kv10.1 is a subunit of a voltage-gated potassium channel and that the identification of Kv10 subunits allows screening for modulators of voltage-gated potassium channels comprising

a Kv10 subunit. Because of the involvement of known Kv channels in regulating various biological processes such as neuronal integration and cell proliferation (see, *e.g.*, page 2, lines 15-23) and also because of the expression pattern of Kv10.1 in the brain, spinal cord, prostate, and retina, it is asserted that these modulators are useful for treating disorders of the central nervous system and for modulating male fertility.

Applicant asserts that the present invention has a specific utility. Specific utility is defined by the MPEP as a utility that is specific to the subject matter claimed. The MPEP explains that applications show sufficient specific utility when applicants disclose a "specific biological activity" and reasonably correlate that activity to a "disease condition." MPEP §§2107.01 and 2107.02. In the present application, Applicant discloses a "disease condition," *i.e.*, altered cytoplasmic potassium concentration, that correlates with a "biological activity," *i.e.*, the opening and closing of the Kv10 channels. This application teaches that the Kv10 channels modulate intracellular potassium concentration. The application further provides methods for identifying modulators of the Kv10 channels capable of modulating potassium influx, *e.g.*, for the treatment of altered biological functions in tissues expressing the Kv10 channels, such as abnormalities found in the retina (*e.g.*, vision disorders) or prostate (*e.g.*, male infertility). Applicant thus submits that the present invention has a specific utility, namely that Kv10 channels can regulate potassium concentrations in the cells of certain tissues, which is clearly specific for the claimed Kv10 channels and not just any ion channels or even any potassium channels.

Applicant also asserts that the present invention has a substantial or "real-world" use. This invention provides Kv10 polypeptides. The application also teaches that Kv10 channels modulate intracellular potassium concentration in certain tissues and teaches how to assay the function of a Kv10 channel and how to identify modulators of Kv10 channels. For example, on pages 42-49 of the specification, assays are provided that can be used to screen for inhibitors and activators of Kv10 channels, *e.g.*, assays that involve measuring current, measuring membrane potential, measuring ion flux, or measuring patch-clamp electrophysiology. The present invention therefore has a real-world use in the modulation of

intracellular potassium concentration, as well as in the identification of compounds that modulate Kv10 channels and thus can be useful as therapeutic agents for treating diseases related to altered functions in tissues expressing Kv10 channels, such as disorders of the central nervous system.

Finally, Applicant contends that the asserted utility of the present invention is credible, *i.e.*, would be believable to one of skill in the art. An ordinarily skilled artisan, after reading this application, would know (a) how to identify Kv10 potassium channels; (b) how to identify modulators of Kv10 channels; and (c) how to use these modulators so identified to modulate cellular potassium concentration and therefore cellular function in relevant tissue. Because many currently marketed drugs treat a wide variety of diseases or conditions by targeting ion channels, one skilled in the art would believe that the identification of a new potassium channel is useful for developing new therapeutics.

The Examiner's Rejection Is Not Supported by Objective Reasons

In the Office Action mailed March 2, 2006, the Examiner alleged that the instant specification fails to indicate a well-established utility or a specific and substantial asserted utility of the claimed invention. As the basis of this conclusion, the Examiner stated that since the instant specification does not provide any experimental data or sound scientific reasoning to support the claimed role of Kv10.1 polypeptide as a voltage-gated potassium channel or its association with any disease or disorder, the invention is therefore incomplete and has no patentable use. In particular, the Examiner challenged the credibility of Applicant's assertion of Kv10.1 as a subunit of a voltage-gated potassium channel, relying on the references by Skolnick *et al.* and Bork *et al.* See the first paragraph on page 4 of the Action.

Yet, the Examiner's reliance is misplaced. First and foremost, Applicant's experiments have already shown the Kv10.1 polypeptide can, when coupled with a Kv2.1 or Kv2.2 subunit, form a functional heteromultimeric voltage-gated potassium channel. See Example 2 on page 63 of the specification. Applicant's assertion that Kv10.1 is a subunit of a voltage-gated potassium channel is therefore supported by experimental evidence; it is not a mere speculation.

Secondly, even if the functionality of Kv10.1 had not been proven by experimental evidence, the Skolnick and Bork references still would not directly challenge the credibility of the asserted role of Kv10.1 as a subunit of a voltage-gated potassium channel. This is because these references are not immediately relevant to the credibility of Kv10's asserted role as a subunit of a voltage-gated potassium channel and therefore do not provide reasonable support for the Examiner's doubts about the credibility of the asserted utility of the claimed invention. For example, the Bork *et al.* and Skolnick *et al.* references provide some general discussions about the pitfalls in predicting protein function on the basis of amino acid sequence homology. Applicant does not dispute these general statements. It must be noted, however, that ion channels have been the focus of intensive research for at least the last two decades. There exists an abundance of knowledge of well-defined ion channel families and the common structural features for each family. For instance, the conserved region of a voltage-gated potassium channel contains the signature six transmembrane domains, arranged in a distinct pattern (see, *e.g.*, page 1, lines 23-27, of the specification). This is precisely why there is a much higher likelihood, if not a near certainty, that a new member of a ion channel family can be correctly recognized based on sequence homology and distinct structural features. The Bork and Skolnick references simply do not address this particular consideration. Applicant contends that, given the state of the art in the field of ion channel research, a sequence homology set forth in the present application (*e.g.*, Figure 1) is sufficient to support a conclusion that Kv10.1 belongs to the voltage-gated Kv potassium channel family.

Taken together, the asserted role of Kv10.1 as a voltage-gated potassium channel has been confirmed by experimental evidence. The references cited by the Examiner do not contradict this conclusion. No evidence or reasoning has been provided to challenge the credibility of Applicant's assertion that modulators of a voltage-gated potassium channel comprising a Kv10 subunit can be used for treating a variety of conditions such as disorders of the central nervous system. Accordingly, Applicant contends that the rejection under 35 U.S.C. §101 is improper as the presumption of utility is not overcome.

The Utility Rejection Contradicts the Allowance of the Parent Application

Lastly, Applicant notes that USSN 09/833,466, of which this application is a division, has already issued as U.S. Patent No. 6,727,353. Considering the fact that the two applications have the same specification, one claiming the Kv10 polynucleotide and the other the Kv10 polypeptide, the utility rejection in this application is in direct contradiction with the patentable utility apparently recognized in the parent application. To sustain this rejection would create a significant inconsistency in the PTO's treatment of this invention.

Summary

In summary, Applicant does not believe that the utility rejection is proper and therefore respectfully requests its withdrawal.

B. 35 U.S.C. §112, First Paragraph

Utility-Based Enablement Rejection

Claims 12-18 were also rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement due to the lack of patentable utility as required by 35 U.S.C. §101. As stated in the section above, the claimed invention fully complies with the utility requirement under 35 U.S.C. §101, Applicant contends that the enablement rejection on this ground is improper and respectfully requests its withdrawal.

Written Description Rejection

Claims 12-15, 17, and 18 were also rejected under 35 U.S.C. §112, first paragraph, for alleged inadequate written description. Specifically, the Examiner asserted that the specification does not provide sufficient description of the claimed genus of polypeptides. Applicant respectfully traverses the rejection in light of the present claim amendment.

Possession of claimed invention may be shown by a variety of descriptive means, including words, structure, figures, diagrams, and formulas. MPEP §2163 I. Case law provides more specific guidance in setting the standard for written description.

The amended claims 12 and its dependent claims are directed to an isolated polypeptide that comprises an alpha subunit of a Kv potassium channel. The claimed polypeptide forms a voltage-gated Kv potassium channel with at least one additional Kv alpha subunit, and comprises an amino acid sequence at least 90% identical to SEQ ID NO:3.

These claims fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993).

In addition, proper description of functional features of a claimed invention can play an important role in satisfying the written description requirement. The Federal Circuit recently stated that "*Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

With regard to the claimed Kv10 polypeptides, pending claims set forth both functional features, *e.g.*, capable of forming a voltage-gated Kv potassium channel with at least one additional Kv alpha subunit, and structural features, *e.g.*, comprising an amino acid sequence that is at least 90% identical to one reference sequence (SEQ ID NO:3). As is generally recognized, having a certain level of sequence homology to a reference sequence is a physical/structural property of a claimed polypeptide, because such homology relies upon the amino acid sequence of the polypeptide. Hence, the pending claims set forth commonly shared structural features of the claimed Kv10 polypeptides.

Commonly shared functional features of the claimed Kv10 polypeptides are also provided: when combined with at least another Kv alpha subunit, each Kv10 polypeptide can

form a Kv potassium channel with the characteristic of voltage-gating. These functional features can be readily tested by one of ordinary skill in the art using well-established, routinely practiced techniques as well as according to the teaching of the present specification (*see, e.g.*, Example 2 on page 63).

Thus, both structural and functional features commonly shared by the claimed genus of Kv10 polypeptides have been described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The description in this application is consistent with the standards set forth in both *Lilly* and *Amgen*.

To support the conclusion that the claims are not adequately described, the Examiner argued that the specification does not identify any particular portion of the polypeptide should be conserved or provide a representative number of species of the claimed genus of Kv10 polypeptides. Applicant respectfully disagrees. First, the specification does identify a particular portion within SEQ ID NO:3 that should be preserved in order to preserve the functionality. As discussed on page 62, lines 3-18, and as shown in Figure 1, the 102-514 region of SEQ ID NO:3 is where the highest sequence homology is observed when SEQ ID NO:3 is aligned against Kv2.1 and Kv2.2, two distantly related members of the Kv superfamily. Thus, one of skill in the art would know that amino acid residues in this region, particularly those in the shaded areas of Figure 1, are likely preserved for functionality. Second, additional species of Kv10 polypeptides such as polymorphic variants are described in the specification, *e.g.*, on page 10, lines 16-22. These points favor a finding of adequate written description of the claimed invention.

Furthermore, the Examiner cited *Fiddes v. Baird*, 30 USPQ2d 1481 (Bd. Pat. App. & Int. 1993) to buttress the contention that the pending claims are insufficiently described. The Board ruled in *Fiddes* that adequate written description was not present to support a broad claim drawn to mammalian fibroblast growth factors (FGF) when only bovine pituitary FGF amino acid sequence and its theoretical nucleotide sequences were disclosed. Examiner apparently was of the opinion that the facts in *Fiddes* are analogous to that in the present case, such that a finding of inadequate written description in the present application is warranted.

Applicant cannot agree with the Examiner's reading of the *Fiddes* case and application of *Fiddes* in the present application.

First, *Fiddes v. Baird* is not inconsistent with the standards for written description as set forth by *Lilly* or *Fiers*. In fact, the Board in *Fiddes* quoted *Fiers* in the discussion of what constitutes adequate written description. 30 USPQ2d at 1483. Moreover, the *Lilly* decision was handed down later in time than *Fiddes* (1997 v. 1993) and by a higher legal authority (Federal Circuit v. the Board). Thus, even if any inconsistency existed, the *Lilly* decision would be controlling over *Fiddes*.

Second, the fact pattern of *Fiddes* is not analogous to that of the present case. In *Fiddes*, a broad claim was drawn to mammalian FGF based on the specification disclosing a bovine FGF amino acid sequence and a ***deduced*** nucleotide sequence, but not any naturally occurring FGF nucleotide sequence. As it later turned out, the deduced nucleotide sequence disclosed in the specification is significantly different from the naturally occurring FGF nucleotide sequence, largely due to codon degeneracy. In essence, the patent applicants in *Fiddes* sought to patent a large genus of polypeptides and polynucleotides when they did not have in their possession any correct polynucleotide sequence. The Board's finding of inadequate written description was based on the notion that the claim of a genus of polynucleotides cannot be adequately supported when only an ***inaccurate*** polynucleotide sequence was disclosed. The Board in *Fiddes* did not take the position that the claim of a genus cannot be adequately supported by the disclosure of an ***accurate*** polynucleotide sequence. Nor could the Board, under *Lilly*, properly require the claim of a genus to be supported by the patent applicant's possession of every embodiment of the genus.

In contrast to *Fiddes*, inventor of the present application had in his possession both the amino acid sequence of a Kv10 subunit of a voltage-gated potassium channel and the naturally occurring Kv10 nucleotide sequence encoding the subunit in full length (SEQ ID NOs: 2 and 3). In addition, the claims in the present application are not drawn to a broad genus of molecules without specific structural or functional definition (such as simply reciting "mammalian Kv channel subunits"). As discussed above, both structural and functional features

commonly shared by the claimed genus have been described in detail, which reasonably convey to one of skill in the art that Applicant had the claimed invention in his possession.

Taken together, the disclosure in the present application provides both the structural/physical features and functional characteristics of the claimed genus of Kv10 polypeptides, fully satisfying the written description requirement under *Lilly* and *Fiers*. On the other hand, there exist crucial factual distinctions between the present case and *Fiddes v. Baird*, which would make it improper to apply *Fiddes* mechanically. As such, Applicant respectfully requests that the Examiner withdraw the written description rejections.

C. 35 U.S.C. §112, Second Paragraph

Claims 12-18 were further rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness. Applicant respectfully traverses the rejection in light of the present claim amendment.

First, the Examiner rejected claims 12 and 15 for reciting the term "Kv10.1," alleging that the term is indefinite because it is not defined based on its amino acid sequence. Applicant does not agree with the Examiner, because the specification indeed provides a clear definition for this term, *see, e.g.*, page 12, line 23, to page 13, line 6. To expedite prosecution, however, this term has been replaced with "Kv," which Applicant believes is a term commonly understood by those of skill in the art to refer to a well defined family of voltage-gated potassium channels, *see, e.g.*, page 2, lines 15-30, of the specification.

Second, the Examiner rejected claim 12 for reciting the term "subsequence." This term has now been replaced with "an amino acid sequence," which Applicant believes is without any ambiguity.

Third, the Examiner rejected claim 18 for reciting the term "the nucleic acid" without proper antecedent basis. The objected-to language has been deleted from this claim.

Fourth, claims 13, 14, 16, and 17 were rejected for dependency from rejected base claims. Since all of the above indefiniteness rejections have been overcome, Applicant submits that this rejection is now moot.

The rejection under 35 U.S.C. §112, second paragraph, is fully addressed. The withdrawal of the rejection is thus respectfully requested.

D. Double Patenting Rejection

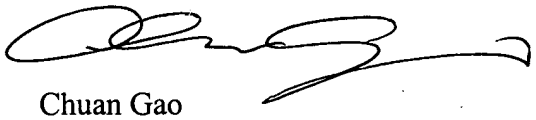
The Examiner contended that, if claim 12 is found patentable, claim 13 will be objected to for double patenting. Since claim 13 has now been amended to be clearly distinct from claim 12, this rejection is moot.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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